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Docket No: 3322/1H702US1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Joanne MEYERS; Rory BARRINGTON-MARTIN; Alex PARKER

Serial No.: 09/935,464

Art Unit: 1655

Confirmation No.: 9495

Filed: August 23, 2001

Examiner: Jeanine Anne Goldberg

For: METHODS AND COMPOSITIONS FOR DIAGNOSING AND TREATING  
NEUROPSYCHIATRIC DISORDERS SUCH AS SCHIZOPHRENIA

PRELIMINARY AMENDMENT AND  
RESPONSE TO RESTRICTION REQUIREMENT

Hon. Commissioner of Patents and Trademarks  
Washington, DC 20231

Sir:

In response to the Official Action dated August 26, 2002 for this application and in accordance with Rule 115 of the Rules of Practice, please enter the following preliminary amendments and consider the accompanying remarks.

Applicants are also submitting herewith: (1) a Petition for Extension of Time, requesting that the deadline for responding to the Official Action be extended for a period of three months (*i.e.*, from September 26, 2002 up to and including December 26, 2002) and accompanied by the appropriate Extension Fee; and (2) an Amendment Transmittal letter, accompanied by the appropriate fee (if any is in fact owed) for the amendments made here.

It is believed that no additional fees are required for these submissions. However, should the U.S. Patent and Trademark Office determine that any fee is owed or that any refund is due for this application, the Commissioner is authorized and requested to charge the fee(s) owed and/or credit the refund(s) due to our Deposit Account No. 04-0100.

Please amend the application as follows:

**IN THE CLAIMS:**

Cancel claims 1-62, without admission or prejudice.

Add new claims 63-101 as follows:

63. (new) An isolated nucleic acid comprising a nucleotide sequence, or the complement thereof, of a polymorphic region of a CADPKL nucleic acid,

which CADPKL nucleic acid has a reference nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2 and SEQ ID NO:4; and

wherein said polymorphic region is indicative of a neuropsychiatric disorder.

64. (new) An isolated nucleic acid according to claim 63, wherein the polymorphic region comprises a single nucleotide polymorphism (SNP).

65. (new) An isolated nucleic acid according to claim 64, wherein the nucleic acid comprises the nucleotide sequence set forth in any one of SEQ ID NOS:37-42 and SEQ ID NOS:77-90, or the complementary sequence thereof.

66. (new) An isolated nucleic acid according to claim 65, wherein the nucleic acid comprises the nucleotide sequence set forth in SEQ ID NO:39 or the complementary sequence thereof.

67. (new) An isolated nucleic acid according to claim 63, wherein the polymorphic region comprises a microsatellite repeat.

68. (new) An isolated nucleic acid according to claim 67, wherein the microsatellite repeat is selected from the group consisting of: 272L16CA2P, 272L16TC1P, 272L16CA4P, D1S471, 272L16TC2P, D1S491, 272L16AATTG7P, 272L16CA6P, and cadpk1mp.

69. (new) An isolated nucleic acid according to claim 68, wherein the microsatellite repeat is 272L16CA2P.

70. (new) An isolated nucleic acid according to claim 68, wherein the microsatellite repeat is 272L16TC1P.

71. (new) An isolated nucleic acid according to claim 68, wherein the microsatellite repeat is 272L16TC2P.

72. (new) An isolated nucleic acid according to claim 68, wherein the microsatellite repeat is 272L16AATTG7P.

73. (new) An isolated nucleic acid according to claim 68, wherein the microsatellite repeat is 272L16CA6P.

74. (new) An isolated nucleic acid according to claim 68, wherein the microsatellite repeat is cadpkImp.

75. (new) A kit for detecting a polymorphic region of a CADPKL nucleic acid,  
said CADPKL nucleic acid having a reference nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2 and SEQ ID NO:4, and  
said kit comprising:

(a) an isolated probe capable of specifically hybridizing to the polymorphic region of said CADPKL nucleic acid or its complement; or  
(b) an isolated primer capable of specifically amplifying the polymorphic region of said CADPKL nucleic acid or its complement,  
wherein the polymorphic region is indicative of a neuropsychiatric disorder.

76. (new) A kit according to claim 75, wherein the polymorphic region of said CADPKL nucleic acid is a single nucleotide polymorphism (SNP).

77. (new) A kit according to claim 76, wherein the polymorphic region of said CADPKL nucleic acid comprises the nucleotide sequence set forth in any one of SEQ ID NOS:37-42 and SEQ ID NOS:77-90, or the complementary sequence thereof.

78. (new) A kit according to claim 77, wherein the polymorphic region of said CADPKL nucleic acid comprises the nucleotide sequence set forth in SEQ ID NO:39 or the complementary sequence thereof.

79 (new) A kit according to claim 75, wherein the polymorphic region of said CADPKL nucleic acid comprises a microsatellite repeat.

80. (new) A kit according to claim 79, wherein the microsatellite repeat is selected from the group consisting of: 272L16CA2P, 272L16TC1P, 272L16CA4P, D1S471, 272L16TC2P, D1S491, 272L16AATTG7P, 272L16CA6P, and cadpkImp.

81. (new) A kit according to claim 80, wherein the microsatellite repeat is 272L16CA2P.

82. (new) A kit according to claim 80, wherein the microsatellite repeat is 272L16TC1P.

83. (new) A kit according to claim 80, wherein the microsatellite repeat is 272L16TC2P.

84. (new) A kit according to claim 80, wherein the microsatellite repeat is 272L16AATTG7P.

85. (new) A kit according to claim 80, wherein the microsatellite repeat is 272L16CA6P.

86. (new) A kit according to claim 80, wherein the microsatellite repeat is cadpkImp.

87. (new) A kit according to claim 75, wherein

(a) said kit comprises an isolated probe capable of specifically hybridizing to the polymorphic region of said CADPKL nucleic acid or its complement; and

(b) said probe comprises the nucleotide sequence set forth in any one of SEQ ID NOS:37-42 and SEQ ID NOS:77-90, or the complementary sequence thereof.

88. (new) A kit according to claim 87, wherein the probe comprises the nucleotide sequence set forth in SEQ ID NO:39 or the complementary sequence thereof.

89. (new) A kit according to claim 75, wherein

(a) said kit comprises at least a first isolated primer capable of specifically amplifying the polymorphic region of said CADPKL nucleic acid or its complement; and

(b) said first isolated primer comprises the nucleotide sequence set forth in any one of SEQ ID NOS:8-35 and SEQ ID NOS:51-76, or the complementary sequence thereof.

90. (new) A kit according to claim 89 further comprising a second isolated primer capable of specifically amplifying the polymorphic region of said CADPKL nucleic acid or its complement,



said second isolated primer comprising the nucleotide sequence set forth in any one of SEQ ID NOS:8-35 and SEQ ID NOS:51-76, of the complementary sequence thereof.

91. (new) A kit according to claim 75, wherein said kit comprises an isolated first primer and an isolated second primer capable of amplifying the polymorphic region of said CADPKL nucleic acid or its complement said first and second primers being selected from the group consisting of:

(a) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:8 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:9 or its complement;

(b) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:10 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:11 or its complement;

(c) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:12 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:13 or its complement;

(d) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:14 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:15 or its complement;

(e) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:16 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:17 or its complement;

(f) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:18 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:19 or its complement;

(g) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:20 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:21 or its complement;

(h) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:22 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:23 or its complement;

(i) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:24 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:25 or its complement;

(j) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:26 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:27 or its complement;

(k) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:28 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:29 or its complement;

(l) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:30 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:31 or its complement;

(m) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:32 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:33 or its complement;

(n) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:34 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:35 or its complement;

(o) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:51 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:52 or its complement;

(p) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:53 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:54 or its complement;

(q) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:55 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:56 or its complement;

(r) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:57 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:58 or its complement;

(s) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO: 59 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:60 or its complement;

(t) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:61 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:62 or its complement;

(u) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:63 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:64 or its complement;

(v) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:65 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:66 or its complement;

(w) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:67 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:68 or its complement;

(x) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:69 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:70 or its complement;

(y) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:71 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:72 or its complement;

(z) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:73 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:74 or its complement; and

(aa) a first nucleic acid having the nucleotide sequence set forth in SEQ ID NO:75 or its complement, and a second nucleic acid having the nucleotide sequence set forth in SEQ ID NO:76 or its complement.

92. (new) A kit according to claim 91, wherein

(i) the first primer comprises the nucleotide sequence set forth in SEQ ID NO:12 or its complement; and

(ii) the second primer comprises the nucleotide sequence set forth in SEQ ID NO:13 or its complement.

93. (new) A kit according to claim 91, wherein

(i) the first primer comprises the nucleotide sequence set forth in SEQ ID NO:20 or its complement; and

(ii) the second primer comprises the nucleotide sequence set forth in SEQ ID NO:21 or its complement.

94. (new) A kit according to claim 91, wherein

(i) the first primer comprises the nucleotide sequence set forth in SEQ ID NO:22 or its complement; and

(ii) the second primer comprises the nucleotide sequence set forth in SEQ ID NO:23 or its complement.

95. (new) A kit according to claim 91, wherein

(i) the first primer comprises the nucleotide sequence set forth in SEQ ID NO:28 or its complement; and

(ii) the second primer comprises the nucleotide sequence set forth in SEQ ID NO:29 or its complement.

96. (new) A kit according to claim 91, wherein

(i) the first primer comprises the nucleotide sequence set forth in SEQ ID NO:32 or its complement; and

(ii) the second primer comprises the nucleotide sequence set forth in SEQ ID NO:33 or its complement.

97. (new) A kit according to claim 91, wherein

(i) the first primer comprises the nucleotide sequence set forth in SEQ ID NO:34 or its complement; and

(ii) the second primer comprises the nucleotide sequence set forth in SEQ ID NO:35 or its complement.

98. (new) An isolated nucleic acid comprising the nucleotide sequence set forth in any one of SEQ ID NOS:37-42 and SEQ ID NOS:77-90, or the complementary sequence thereof.

99. (new) An isolated nucleic acid according to claim 98 which comprises the nucleotide sequence set forth in SEQ ID NO:39 or the complementary sequence thereof.

100. (new) An isolated nucleic acid comprising the nucleotide sequence set forth in any one of SEQ ID NOS:8-35 and SEQ ID NOS:51-76, or the complementary sequence thereof.

101. (new) An isolated nucleic acid according to claim 100 which comprises the nucleotide sequent set forth in any one of SEQ ID NOS:12-13, 20-21, 22-23, 28-29, 32-33 or 34-35 or the complementary sequence thereof.

#### **REMARKS**

Claims 1-62 were original filed with and pending in this application. Claims 1-62 have been canceled in the above amendment, without admission and without prejudice to Applicants' right to pursue the subject matter of those canceled claims in either this or other (*e.g.*, related) patent applications. New claims 63-101 have been added to more particularly specify the elected subject matter of Applicants invention. No new matter has been introduced. Entry and consideration of these new claims are therefore respectfully submitted.

#### **Restriction Requirement**



The Office Action requires a restriction of the original pending claims to one of the following groups:

- Group I. Claims 1-41, and 54-72, drawn to nucleic acids which comprise a polymorphic region of CADPKL, a kit containing probes/primers, methods of detecting the polymorphism, and methods of determining whether a subject is at risk of developing a neuropsychiatric disorder;
- Group II. Claims 42-43, drawn to a method of selecting an appropriate drug for administration; and
- Group III. Claims 44-53, drawn to a method of treating a subject having a disease or disorder.

In addition, the Office Action indicates that a single polymorphism (for example, a single SNP) must also be elected for examination. Applicants note with appreciation, however, that the examination of such an elected polymorphism may include its complement and/or subsequences, including

oligomeric probes and/or primers. See, in particular, lines 4-8 on page 4 of the Office Action.

In order to be fully responsive to the Requirement for Restriction, Applicants hereby provisionally elect with traverse to prosecute the claims of Group I. It is noted that the original claims encompassed by Group I (*i.e.*, claims 1-41 and 54-72) have been canceled without prejudice or admission in this Preliminary Amendment and new claims 63-100 have been introduced. It is believed that all of these new claims are directed to the subject matter of elected Group I. Applicants also provisionally elect, with traverse, for these claims to be examined with respect to the particular CADPKL polymorphism referred to in this application as cadpk17 and comprising the nucleotide sequence set forth in SEQ ID NO:39. Applicants note, however, that the pending claims also recite particular oligonucleotide sequences disclosed in this application as being particularly useful for amplifying and/or detecting the cadpkly7 polymorphism. These include SEQ ID NOS:12 and 13 recited in claims 89-92, 100, and 101. Applicants therefore understand that claims specifying these particular sequences will be examined in this application along with claims specifically reciting the cadpkly7 polymorphism and/or SEQ ID NO:39.

**Traversal of the Restriction Requirement:**

The above election is provisionally made in order to be fully responsive to the Office Action. However, Applicants respectfully traverse the Requirement for Restriction and reserve the right to petition therefrom under 37 C.F.R. § 1.144.

Contrary to what is stated in the Office Action, the polymorphisms recited in the claims of this application are related by at least one common inventive concept. In particular, all variants of a single nucleic acid (CADPKL) that correlate with, and are therefore indicative of, neuropsychiatric disorders such as schizophrenia. Thus, the claims are all united by Applicants discovery that the CADPKL gene, and variations thereof, are useful for diagnosing and treating such disorders.

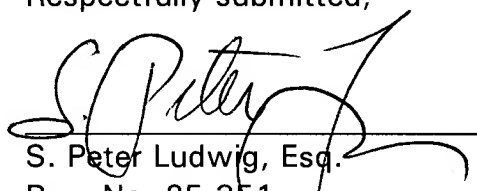
Moreover, 37 C.F.R. § 1.146 provides that, where an application contains a generic claim to a generic invention (for example claim 63 and 64, introduced in this Preliminary Amendment), the Applicants may pursue claims to both the generic invention and for a reasonable number of species. For all of the foregoing reasons, Applicants again respectfully submit that the Restriction between individual nucleic acids is improper and should be withdrawn in favor of a species election requirement. In so doing, Applicants respectfully request that the above election of cadpk17 be treated as a species election.

## Conclusion

For all of the foregoing reasons, Applicants respectfully request that the Requirement for Restriction be withdrawn and that claims 63-101 *all* be examined in this application. Alternatively, Applicants request that the restriction to a single polymorphism be treated as a species election requirement and the cadpk17 be examined as a species encompassed by generic claims 63-64, 75-76.

Respectfully submitted,

Dated: December 23, 2002

  
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